
Direct Exposure to SARS-CoV-2 and Cigarette Smoke Increases Infection Severity and Alters the Stem Cell-Derived Airway Repair Response.

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Public Summary:

Current smoking is associated with increased risk of severe COVID-19, but it is not clear how cigarette smoke (CS) exposure affects SARS-CoV-2 airway cell infection. We directly exposed air-liquid interface (ALI) cultures derived from primary human nonsmoker airway basal stem cells (ABSCs) to short term CS and then infected them with SARS-CoV-2. We found an increase in the number of infected airway cells after CS exposure with a lack of ABSC proliferation. Single-cell profiling of the cultures showed that the normal interferon response was reduced after CS exposure with infection. Treatment of CS-exposed ALI cultures with interferon beta-1 abrogated the viral infection, suggesting one potential mechanism for more severe viral infection. Our data show that acute CS exposure allows for more severe airway epithelial disease from SARS-CoV-2 by reducing the innate immune response and ABSC proliferation and has implications for disease spread and severity in people exposed to CS.

Scientific Abstract:

Current smoking is associated with increased risk of severe COVID-19, but it is not clear how cigarette smoke (CS) exposure affects SARS-CoV-2 airway cell infection. We directly exposed air-liquid interface (ALI) cultures derived from primary human nonsmoker airway basal stem cells (ABSCs) to short term CS and then infected them with SARS-CoV-2. We found an increase in the number of infected airway cells after CS exposure with a lack of ABSC proliferation. Single-cell profiling of the cultures showed that the normal interferon response was reduced after CS exposure with infection. Treatment of CS-exposed ALI cultures with interferon beta-1 abrogated the viral infection, suggesting one potential mechanism for more severe viral infection. Our data show that acute CS exposure allows for more severe airway epithelial disease from SARS-CoV-2 by reducing the innate immune response and ABSC proliferation and has implications for disease spread and severity in people exposed to CS.

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